



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

re: Dolly et al.

Serial Number: 09/676,053

Filed: September 28, 2000

For: MODIFICATION OF CLOSTRIDIAL
TOXINS AS TRANSPORT PROTEINS

) Examiner: ZEMAN, ROBERT

) Group Art Unit: 1645

CERTIFICATE OF MAILING OR FACSIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the Patent and Trademark Office fax number 571-273-8300, or mailed by first class mail to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below.

Date: May 30, 2007

Name: Shawwna Waddell

Reply and Amendment

BOX RCE

Commissioner for Patents
Box 1450
Alexandria, VA 20231

Dear Sir,

In reply to the Office Action of January 3, 2007, Applicant have the following comments.

The Status of the Claims begins on page 2.

The Remarks begin on page 6.

STATUS OF THE CLAIMS

This claim listing shall supercede any prior listing of the claims.

1-30 (Canceled)

31. (Currently amended) A composition comprising an active Clostridial neurotoxin joined to a neuropharmacological agent~~drug or other bioactive molecule~~; wherein the active neurotoxin possesses mouse lethality of 3.3×10^5 LD₅₀/mg or greater and has binding specificity for a target nerve cell, is internalizable by the target nerve cell and has enzymatic activity for a target substrate selected from the group consisting of SNAP-25, VAMP, and Cellubrevin.

32. (Previously presented) The composition of claim 31 wherein the active Clostridial neurotoxin is an active botulinum neurotoxin.

33. (canceled)

34. (Currently amended) The composition of claim 31 wherein said neuropharmacological agent~~drug~~ is an intracellular acting drug.

35. (Previously presented) The composition of claim 32 wherein said Clostridial neurotoxin is selected from the group consisting of a botulinum toxin A, a botulinum toxin

B, a botulinum toxin C1, a botulinum toxin D, a botulinum toxin E, a botulinum toxin F, and a botulinum toxin G.

36. (Currently amended) The composition of claim 31 wherein said neuropharmacological agent~~drug~~ is selected from the group consisting of a protein synthesis toxin, an inhibitor of neurotransmitter release, neuronal calcium channel blocker, a ribozyme and an oligonucleotide.
37. (Previously presented) The composition of claim 31 wherein the active Clostridial neurotoxin is an active tetanus neurotoxin.
38. (Currently amended) A pharmaceutical composition for treatment of a neuromuscular dysfunction in a mammal, comprising an active Clostridial neurotoxin joined to a neuropharmacological agent~~drug or other bioactive molecule~~; and a pharmaceutically acceptable excipient; wherein the active neurotoxin possesses mouse lethality of 3.3×10^5 LD₅₀/mg or greater and has binding specificity for a target nerve cell, is internalizable by the target nerve cell and has enzymatic activity for a target substrate selected from the group consisting of SNAP-25, VAMP and Cellubrevin.
39. (Previously presented) The pharmaceutical composition of claim 38 wherein the active Clostridial neurotoxin is an active botulinum neurotoxin.

40. (Previously presented) The pharmaceutical composition of claim 38 wherein the active Clostridial neurotoxin is selected from the group consisting of a botulinum toxin A, a botulinum toxin B, a botulinum toxin C1, a botulinum toxin D, a botulinum toxin E, a botulinum toxin F, and a botulinum toxin G.
41. (Previously presented) The composition of claim 38 wherein the active Clostridial neurotoxin is an active tetanus neurotoxin.
42. (Previously presented) The pharmaceutical composition of claim 38 wherein the neuromuscular dysfunction is characterized by uncontrollable muscle spasms.
43. (Currently amended) The composition of either of claims 31 or 38 wherein the neuropharmacological agent~~drug or other bioactive molecule~~ is an inhibitor of neurotransmitter release.
44. (Currently amended) The composition of either of claims 31 or 38 wherein the neuropharmacological agent~~drug or other bioactive molecule~~ is an active ingredient for treatment of botulism or tetanus.
45. (Currently amended) The composition of either of claims 31 or 38 wherein the neuropharmacological agent~~drug or other bioactive molecule~~ is selected from the group consisting of a GABA agonist, a neuronal calcium channel

Serial No. 09/676,053
Reply of May 14, 2007

agonist, an adenosine agonist, a glutamate antagonist, a protein synthesis toxin, a zinc-dependent protease inhibitor, a neuronal growth factor, an antiviral agent, a nicotinic antagonist, a neuronal calcium channel blocker, an acetylcholine esterase inhibitor, a potassium channel activator, a vasamicol inhibitor, a ribozyme and a transcribable gene.